REMARKS

This application contains claims 1-38, the status of which is as follows:

(a) Claims 1-10 have been canceled. The Applicant intends to prosecute these claims in a continuation of another application filed by the Applicant.

(b) Claims 11-38 are new.

No new matter has been added.

Claims 11-38 are new. Claim 11 is supported in the Applicant's specification as follows. The first element of claim 1 reads: "paclitaxel, adapted to be administered to a systemic blood circulation of a patient." The specification discloses paclitaxel as a pharmacological agent with which the techniques of the application may be used: " In particular these embodiments of the present invention may be adapted for use in facilitating the administration of the following pharmacological agents" (p. 12, lines 17 19). The "following pharmacological agents" include "paclitaxel," as indicated in the table entitled "Anti-Neoplastic Agents," in the section labeled "OTHER MEDICATIONS," which appears near the bottom of p. 21. It is clear in numerous places in the specification that the agent may be delivered to the systemic blood circulation. For example, the specification describes an embodiment including "...a chemical agent supplied to a body of a subject. . . the chemical agent is a therapeutic agent" (p. 34, lines 6-12). The "body of a subject" clearly includes the subject's systemic blood circulation, as indicated, for example, by the following:

> Advantageously, this prior generation of heightened concentrations of the drug in the blood tends to provide relatively rapid transfer of the drug across the BBB and into the brain, without unnecessarily prolonging the enhanced permeability of the BBB while waiting for the blood concentration of the drug to reach an appropriate level. Alternatively, for some applications it is desirable to give a single injection of a bolus of the drug shortly before or after initiation of stimulation of the SPG (p. 42, lines 15-20).

The second element of claim 11 reads: "one or more electrodes, adapted to be applied. to a site of the patient selected from the group consisting of: a sphenopalatine ganglion (SPG), and a neural tract originating in or leading to the SPG." This claim

element appears nearly verbatim several times in the specification, including on p. 30, lines 3-5: "one or more electrodes, adapted to be applied to a site selected from a group of sites consisting of: a sphenopalatine ganglion (SPG) of the patient and a neural tract originating in or leading to the SPO."

The third and last element of claims 11 reads: "a control unit, adapted to drive the one or more electrodes to apply a current to the site capable of inducing an increase in a. concentration of the paclitaxel in a brain of the patient." Facilitating drug delivery to the brain is an important aspect of many embodiments disclosed in the specification, as is clear throughout the specification. The following is just one example:

> The middle and anterior cerebral arteries provide the majority of the blood... supply to the cerebral hemispheres, . . . and significant portions of the following structures: the temporal lobes, internal capsule, basal ganglia and thalamus. These structures are involved in many of the neuxological and psychiatric diseases of the brain, and preferred embodiments of the present invention are directed towards providing improved blood supply and drug delivery to these structures (p. 8, lines 10-16).

Support in the Applicant's specification for claims 12-21 is shown in the following table. It is noted that only a single reference in the specification is provided, even for claims which find support in multiple references in the specification.

New claim	Applicant's specification
12. (" induce an increase in permeability to the paclitaxel of a blood-brain barrier (BBB) of the patient, so as to induce the increase in the concentration of The paclitaxel")	". . . the control unit is adapted to configure the current so as to facilitate uptake of a drug through the BBB when the permeability of the BBB is increased" (p. 32, lines 8-10).
13. ("the one or more electrodes are adapted for a period of implantation in the patient greater than about one month")	"Preferably, the one or more electrodes are adapted for a period of implantation in the patient greater than about one month" (p. 30, lines 30-31).
14. ("the control unit is adapted to be implanted in a nasal cavity of the patient")	"Still further alternatively or additionally, the control unit is adapted to be implanted in a nasal cavity of the patient" (p. 31, lines 10-12).

15. ("the one or more electrodes are adapted to be implanted in a nasal cavity of the patient")	"Preferably, the one or more electrodes are adapted to be implanted in a nasal cavity of the patient" (p. 31, lines 13-14).
16. ("at least one of the one or more electrodes comprises a flexible electrode, adapted for insertion through a nostril of the patient and to extend therefrom to the site")	"For some applications, at least one of the one or more electrodes includes a flexible electrode, adapted for insertion through a nostril of the patient and to extend therefrom to the site" (p. 31, lines 14-16).
17. ("at least one biosensor, adapted to measure a physiological parameter of the patient and to generate a signal responsive thereto, wherein the control unit is adapted to modify a parameter of the applied current responsive to the signal")	"The apparatus preferably includes at least one biosensor, adapted to measure a physiological parameter of the patient and to generate a signal responsive thereto. The control unit, in turn, is preferably adapted to modify a parameter of the applied current responsive to the signal" (p. 31, lines 17-20).
18. ("the biosensor comprises a blood flow sensor")	"As appropriate, the biosensor may include one or more of the following: a blood flow sensor" (p. 31, lines 20-22).
19 (lithe biosensor comprises a temperature sensor")	"As appropriate, the biosensor nlay include one or more of the following: . . . a temperature sensor" (p. 31, lines 20-23).
20. ("the biosensor comprises transcranial Doppler (TCD) apparatus")	"As appropriate, the biosensor may include one or more of the following: ... transcranial Doppler (TCD) apparatus" (p. 31, lines 20-23),
21. ("the biosensor is selected from the list consisting of: a chemical sensor, an ultrasound sensor, laser-Doppler apparatus, a systemic blood pressure sensor, an intracranial blood pressure sensor, a kinetics sensor, an electroencephalographic (BEG) sensor")	"As appropriate, the biosensor may include one or more of the following: . . . • a chemical sensor, • an ultrasound sensor. . . • laser-Doppler apparatus. • a systemic blood pressure sensor. • an intracranial blood pressure sensor. . . a • kinetics sensor. . . • an electroencephalographic (BEG) sensor" (p. 31, line 20 - p. 32, line 6).

New claims 22-23 are method claims parallel to apparatus claims 11-12, and are supported in the Applicant's specification as described hereinabove with respect to claims 11-12.

New claim 24 is supported in the Applicant's specification as follows, The first element of claim 24 ("paclitaxel") is supported in the same manner as described hereinabove with respect to claim 11. The second element of claim 24 reads: "an odorant capable of having a neuroexcitatory effect on the sphenopalatine ganglion (SPG) that induces an increase in a concentration of the paclitaxel in a brain of the patient." This element finds support in numerous places in the specification. including "Alternatively or additionally, the changes induced by electrical modulation as described hereinabove are achieved by presenting odorants to an air passage of a patient" (p. 9, lines 24-25). As discussed hereinabove with respect to claim 11, facilitating drug delivery to the brain is an important aspect of many embodiments disclosed in the specification. The neuroexcitatory effect of the odorant on the SPG is supported, for example, by the following:

> There is still further provided, in accordance with a preferred embodiment of the present invention, a chemical agent delivery system including:
>
> a chemical agent supplied to a body of a subject for delivery to a site in a central nervous system of the subject via blood of the subject; and
>
> a stimulator for stimulating parasympathetic fibers associated with the sphenopalatine ganglion, thereby to render a BBB of the subject permeable to the chemical agent during at least a portion of the time that the chemical agent is present in the blood.
>
> In a preferred embodiment, the chemical agent is a therapeutic agent. . . .
>
> Alternatively or additionally, the stimulator includes an odorant stimulator. Preferably, the odorant stimulator includes a neuroexcitatory agent (p. 34, lines 4-19).

The third and last element of claim 24 reads: "odorant presentation apparatus, adapted to present the odorant to an air passage of the patient." This is supported by the following: "The odorant is preferably presented using apparatus known in the art,

such as aqueous spray nasal inhalers; metered dose nasal inhalers; or air-dilution olfactometers" (p. 10, line 32 - p. 11. line 2).

Support in the Applicant's specification for claims 25-36 is shown in the following table. It is noted that only a single reference in the specification is provided, even for claims which find support in multiple references in the specification.

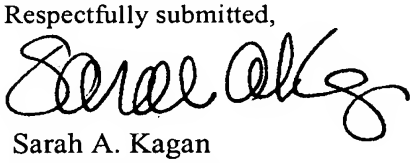
New claim(s)	Applicant' s specification
25. ("induce an increase in permeability to the paclitaxel of a Blood-brain barrier (BBB) of the patient, so as to induce the increase in the concentration of the paclitaxel")	" ... a method is provided to enhance delivery of therapeutic molecules across the BBB by presenting an odorant to an air passage of a. patient, such as a nasal cavity or the throat. In a preferred application, this method serves as a neurological drug delivery facilitator" (p. 10, lines 29-33).
26,27, and 28. ("aqueous spray" "nasal inhaler," "metered dose nasal inhaler," and "an air-dilution olfactometer," respectively)	"The odorant is preferably presented using apparatus known in the art, such as aqueous spray nasal inhalers; metered dose nasal inhalers; or air-dilution olfactometers" (p. 10, line 32 - p. 11, line 2).
29 and 30. ("the air passage includes a nasal cavity of the patient." and "the air passage includes a throat of the patient," respectively)	" ... presenting odorants to an air passage of a patient, such as a nasal cavity or the throat" (p. 9, lines 25-26).
31. ("propionic acid, cyclohexanone, and amyl acetate")	"Odorants . . . include, but are not limited to, propionic acid, cyclohexanone, amyl acetate. . ." (p. 10, lines 23-25).
32. ("acetic acid, citric acid, carbon dioxide, sodium chloride, and ammonia")	"Odorants. . . include, but are not limited to, . . . acetic acid. citric acid, carbon dioxide, sodium chloride, ammonia. . ." (p. 10, lines 23. 25).
33. ("menthol, alcohol, nicotine, piperine, gingerol, zingerone, allyl isothiocyanate, cinnamaldehyde, cuminaldehyde, 2-propenyl/2-phenylethyl isothiocyanate, thymol, and eucalyptol")	"Odorants. . . include, but are not limited to.... menthol, alcohol, nicotine, piperine, gingerol, zingerone, allyl isothiocyanate, cinnamaldehyde, cuminaldehyde, 2-propenyl/2-phenylethyl isothiocyanate, thymol. and eucalyptol. . ." (p. 10, lines 23-28).
34. ("the paclitaxel is mixed with the odorant")	"Delivery of a drug can be achieved by mixing the drug with the odorant. . .11 (p. 11. lines 6-7).

35. ("intravenous administration, intraperitoneal administration, and intramuscular administration")	"Delivery of a drug can be achieved. . . by intravenously, intraperitoneally, or intramuscularly administering the drug. . ." (p. 11, lines 6-8).
36. ("a local analgesic mixed with the odorant ")	"For some applications, it is desirable to combine a local analgesic with the odorant. . ." (p. 11, lines 8-9).

New claims 37-38 are method claims parallel to apparatus claims 24-25, and are supported in the Applicant's specification as described hereinabove with respect to claims 24-25.

Notice of allowance of the present application is respectfully requested.

Respectfully submitted,



Sarah A. Kagan
Registration No.32, 141

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SAK/sdm